

Development of a scalable, practical, and transferable GMP-compliant suspension culture-based differentiation process for cardiomyocyte production from human embryonic stem cells.

Grant Award Details

Development of a scalable, practical, and transferable GMP-compliant suspension culture-based differentiation process for cardiomyocyte production from human embryonic stem cells.

Grant Type: Tools and Technologies III

Grant Number: RT3-07838

Project Objective: Develop a disposable rocker bag suspension culture production system that is scalable, practical, transferable and GMP-compliant for the expansion of human embryonic stem cells and their differentiation process (using disposable rocker bag systems) to cardiomyocytes.

Investigator:

Name:	Joseph Gold
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Name:	Chang-Yi "Vincent" Chen
Institution:	City of Hope, Beckman Research Institute
Type:	Co-PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$891,518

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Grant Application Details

Application Title: Development of a scalable, practical, and transferable GMP-compliant suspension culture-based differentiation process for cardiomyocyte production from human embryonic stem cells.

Public Abstract: As ongoing CIRM-funded development of regenerative medicine (RM) progresses, the demand for increasing numbers of pluripotent stem cells and their differentiated derivatives has also increased. We have established a scalable suspension culture system for the production of large quantities of hESC for banking and to seed production of a number of regenerative medicine cell types, notably retinal pigmented epithelia, neural stem cells, dopaminergic neurons and cardiomyocytes, that support a number of CIRM and NIH-funded groups. In addition, we have adapted this system for the suspension production of several hESC derivative cell types, notably cardiomyocytes. While our system has provided unprecedented production capability for a number of cell products in pre-clinical and imminent clinical studies, it has proven impractical to scale up to the level that will be required for clinical trials for some hESC cell products, notably cardiomyocytes, due to high expected human doses. This project will resolve this scale-up challenge by adapting our suspension cell culture system, that is limited to 1-3L spinner culture flasks, to a more readily scalable and controllable suspension bioreactor system that utilizes "bags" capable of volumes up to 500L. Achieving this objective will remove a key barrier to progressing RM for cardiac applications as well as open the door to large clinical trials and commercialization of other regenerative medicine cell products in the years to come.

Statement of Benefit to California: We have developed GMP-compliant suspension cell culture processes for scalable production of hPSC and derivatives. These processes have been invaluable in our support of CIRM- and NIH-funded regenerative medicine projects, including those with RPE, NSC, DA neurons and cardiomyocytes (CM), as well as for production of GMP banks of hPSC for various projects. Our GMP-compliant suspension culture CM production process has made pre-clinical animal studies and small early clinical trials practical. However, while our current CM system is readily transferred to other groups and is meeting current production requirements, the scale requirements for anticipated high dose clinical trials is beyond the practical limitation of our spinner flask-based system. hPSC and CM are sensitive to changes in shear encountered at every scale-up step and re-optimizing conditions at each step is prohibitively expensive. Our experience using bag-based bioreactors for non-hESC products suggests that scale-up in bags will be more controllable and predictable than spinners or stir-tanks reactors. It is also a readily transferred technology. We propose to adapt our suspension hPSC and CM processes to a bag system, optimize conditions at a small scale, then demonstrate scalability at a moderate scale. Success in this project will remove a key barrier to developing many regenerative medicine products, and in particular those where high human doses are anticipated, such as CM.

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